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Associations of Leg Fat Accumulation with Adiposity-Related Biological Factors and Risk of Metabolic Syndrome

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Abstract

The association between regional fat mass distribution and cardiometabolic risk factors has been inconsistent in the literature, and data for ethnic minority groups, such as non-Hispanic blacks and Hispanics, are lacking. We aimed to examine this association among 8802 US residents who participated in the 1999-2004 US National Health and Nutrition Examination Survey (NHANES). Body composition was measured using dual-energy X-ray absorptiometry (DXA). Leg fat indices included leg fat mass (FM), leg fat mass percent (FM%), leg to whole body FM ratio (leg/whole) and leg to trunk FM ratio (leg/trunk). We evaluated the correlation between leg fat indices and adiposity-related risk factors, as well as the association of these indices with metabolic syndrome (MetS). After adjusting for covariates including age, gender, and trunk FM or trunk FM%, higher leg FM and leg FM% were, in general, correlated favorably with adiposity-related risk factors and associated with lower odds of MetS in all ethnicities, including non-Hispanic whites and blacks and Hispanic groups. In addition, in all multivariate-adjusted models, leg/whole and leg/trunk ratios were strongly associated with lower levels of most risk factors and decreased odds of MetS in these ethnicities (all odds ratios comparing extreme quintiles < 0.1). Our results show that leg fat accumulation is inversely associated with adiposity-related biological factors and risk of MetS in both whites and ethnic groups, suggesting that regional fat distribution plays an important role in the etiology of adiposity-related diseases in these populations.

INTRODUCTION

Over the past three decades, the prevalence of overweight and obesity has tripled in the United States, resulting in a serious public health problem, which has placed a substantial burden on the healthcare system (1). Obesity is an important risk factor for the morbidity and mortality of many chronic diseases. Numerous studies have consistently shown that total body fat, particularly abdominal fat accumulation, has been strongly associated with elevated levels of several cardiometabolic risk factors (1) and increased risk of metabolic syndrome (MetS) (2), type 2 diabetes (3) and cardiovascular disease (CVD) (4). On the other hand, rich data also suggest that fat accumulation in leg or other peripheral regions

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DISCLOSURE
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may possess potentially beneficial effects on cardiometabolic health,(5-18) although these studies were conducted primarily among whites or Asians. It is largely unknown whether leg fat distribution is associated with cardiometabolic outcomes among other ethnicities with different body fat distribution and metabolic risk, such as non-Hispanic blacks or Hispanics. (1, 19)

Recently, we found significant correlations between whole body and trunk fat mass (FM) or fat mass percent (FM%) as directly measured using dual-energy X-ray absorptiometry (DXA) with obesity-related biological factors among more than 8000 adults in the National Health and Nutrition Examination Surveys (NHANES) (20). In the current investigation, we utilized the same data to comprehensively examine various leg fat indices in relation to adiposity-related factors and risk of MetS by ethnicity in this large nationally representative sample of US adults.

METHODS AND PROCEDURES

Study population

This study was conducted using data from 3 representative cross-sectional NHANES surveys (1999-2004) that included 31 126 individuals randomly selected from the total civilian, noninstitutionalized US population. African Americans, Mexican Americans, and elderly residents were oversampled to provide more accurate estimates of their characteristics, and each respondent was assigned a weight based on geographic and demographic characteristics to allow for the calculation of population-based estimates. The NHANES sample design and data collection methods have been described in detail elsewhere (21). All procedures were approved by the National Center for Health Statistics Institutional Review Board, and all subjects provided written informed consent.

The present analysis was restricted within NHANES adult participants ≥20 years who were eligible to DXA assessments (n = 14 213). Of these participants, we excluded participants with missing DXA measurements (n = 1122) and participants who took medications for hypertension, high cholesterol or diabetes as these medications can obscure the correlations of interest (n = 4020). We further excluded a small proportion of participants (n = 269) who were not non-Hispanic whites or blacks or Hispanic groups based on the considerations that this group was heterogeneous with respect to ethnicity and the sample size was small to derive stable statistical estimates. After these exclusions, 8802 participants remained in the analysis, and, of them, 1734 of these participants had one or more missing DXA measurements imputed.

Anthropometry and DXA measurements

Body weight, standing height, and waist circumference were assessed by direct measurement following a standard protocol (21). Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Whole-body DXA scans were performed using a Hologic QDR 4500A fan beam densitometer (Hologic Inc., Bedford, MA). Original DXA scan results were analyzed using Hologic Discovery software, version 12.1 (Hologic Inc., Bedford, MA). Missing DXA data were imputed using sequential regression multivariate imputation. In the current analysis, we evaluated leg FM (kg), leg FM% calculated as leg FM divided by total leg mass (kg), leg to whole-body FM (leg/whole) ratio calculated as leg FM divided by whole body FM, and leg to trunk FM (leg/trunk) ratio calculated as leg FM divided by trunk FM.

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Assessment of cardiometabolic risk factors

Systolic blood pressure (SBP), diastolic blood pressure (DBP), serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triacylglycerol (TG), fasting blood glucose (FBG), fasting serum insulin (FSI), and serum C-reactive protein (CRP) were the cardiometabolic risk factors evaluated in the present analysis (20). Because the amount of missing data varied for these biological factors, to preserve statistical power as much as possible, we used all available data for each of these factors (20). Thus the sample size differed for each factor: n = 8420 for SBP; 8383 for DBP; 8297 for TC and HDL-C; 3782 for LDL-C; 4056 for TG; 4104 for FBG; 4046 for FSI; and 8340 for CRP.

Definition of MetS

We used the modified National Cholesterol Education Program's Adult Treatment Panel III criteria such that participants who had 3 or more of the following conditions were considered to have MetS: waist circumference ≥102 cm in men or ≥88 cm in women; TG level ≥150 mg/dL; HDL-C level <40 mg/dL in men or <50mg/dL in women; SBP ≥130 mmHg or DBP ≥85 mmHg; and FBG ≥100 mg/dL.

Covariates

Demographic characteristics such as age, gender, ethnicity, smoking status, alcohol consumption, and physical activity were ascertained by using questionnaire. Ethnicity was categorized into non-Hispanic white, non-Hispanic black, and Hispanic groups (including Mexican Americans and other Hispanics); education was categorized as high school or below, any college, and college graduate or beyond; smoking status was categorized as nonsmoker, past smoker, or current smoker; alcohol consumption was divided into nondrinker, 1-3 drinks/day, or ≥ 4 drinks/day; and regular moderate-to-vigorous physical activity, self-reported CVD, and family history of diabetes and CVD were categorized as yes or no.

Statistical analysis

We examined all continuous variables for outliers and log-transformed these variables to improve normality. Sampled-weighted partial Pearson correlation coefficients were computed to examine the associations among DXA indices and between leg fat indices and the cardiometabolic risk factors. Multivariate models were adjusted for the above-mentioned covariates, as well as trunk DXA indices. Multivariate logistic regression models were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for MetS according to quintiles of leg FM, leg FM%, and leg/whole and leg/trunk ratios adjusted for the same set of covariates. In logistic regression analyses, we took sample weights and NHANES survey design into consideration by using Stata SVY LOGIT command.

All analyses were conducted in quintuplicate by using 5 imputation datasets and the mean of 5 estimates was calculated to derive a single combined statistical summary. This approach was used to calculate point estimates for correlation coefficients and beta coefficients in logistic regression models. To derive the variance of these point estimates, we applied the following statistical approaches. Within-imputation variance (W) was calculated as the average of 5 individual variance estimates (the variance estimator for Fisher's z transformed Pearson correlation coefficients (22) or the variance estimator for beta coefficients in logistic regression), and the between-imputation (B) variance was calculated as the sample variance of the 5 individual estimates, that is, $B=\sum_{i=1}^{5}\left(Q_i-\overline{Q}\right)^2/4$, in which Q_i was the individual estimate and $\bar{Q}$ was the mean of the five individual estimates. The total variance (T) combined the within- and between-imputation variances as follows: $T=W+\frac{6}{5}\times B$. The

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degrees of freedom were determined using the method of Barnard and Rubin (23). We used 47 (number of primary sampling units minus the number of sampling strata) as the degrees of freedom for complete data (21).

Data were analyzed using SAS, version 9.3 (SAS Institute, Inc., Cary, North Carolina) and STATA, version 11.0 (Stata Corporation, College Station, Texas). To take into account multiple comparisons, we used a Bonferroni-corrected P value less than 0.05 (equivalent to $P < 0.00028$, corresponding to 0.05 divided by 178 comparisons) as the significant level.

RESULTS

Characteristics of study population

The baseline characteristics for the study participants by ethnicity are presented in Table 1. Of the 8802 participants, 50.8% (unweighted percentage; n = 4472) of them were non-Hispanic whites, 30.1% (n = 1683) had Hispanics ethnicity, and the rest 19.1% (n = 2647) were non-Hispanic blacks. These three ethnic groups had various distributions of age, education levels, smoking status, physical activity levels, as well as the cardiometabolic risk markers. In terms of anthropometric measurements, in comparison to non-Hispanic whites, non-Hispanic blacks had higher BMI and lower fat mass percent in whole body, trunk, and leg. Although Hispanics and non-Hispanic whites had similar BMI and whole body fat mass percent, the former ethnic group had higher trunk fat mass percent and lower leg fat mass percent than the latter group.

Correlation among DXA indices

The Pearson correlation coefficients among DXA indices are presented in Supplementary Table 1. These DXA indices were highly correlated with each other: correlation coefficients between the individual DXA indices were in the range of 0.65-0.97 for non-Hispanic whites, 0.73-0.98 for non-Hispanic blacks, and 0.64-0.97 for Hispanic groups. In all three ethnic groups, we found modest correlation coefficients among leg fat indices and trunk fat indices. In addition, we found that leg FM was consistently more strongly correlated with trunk FM than with trunk FM%, and, similarly, leg FM% was more strongly correlated with trunk FM % than trunk FM.

Leg fat and obesity-related risk factors

Supplementary Table 2 shows the correlations between leg fat indices and adiposity-related risk factors by ethnicity after adjusting for age, gender, education, and lifestyle factors. In this analysis, in general, leg FM and leg FM% tended to correlate unfavorably with the majority of the risk factors in all three ethnic groups, although the strength of correlations varied across the three groups. In addition, the correlations of leg FM or leg FM% with HDL-C, fasting insulin and CRP levels were particularly strong.

Trunk fat may confound the correlation between leg fat and the biological factors because trunk fat was strongly correlated with both leg fat and the factors. Therefore, we further adjusted for trunk indices (adjusted for trunk FM in analyses for leg FM, and adjusted for trunk FM% in analyses for leg FM% based on the findings in Supplementary Table 1) to examine the independent correlations between leg fat indices and the biological factors, and results are shown in Table 2. After such an adjustment, the direction of the correlations of leg FM and leg FM% was reversed for most of these risk factors, although the majority of these correlations did not achieve statistical significance, except that in non-Hispanic whites and Hispanic groups leg FM and FM% were significantly correlated with HDL-C and/or TG levels. In contrast, leg/whole and leg/trunk ratios were correlated favorably with the risk factors (Table 2), and most of these correlations achieved statistical significance with a few

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exceptions: in non-Hispanic blacks the ratios were non-significantly correlated with LDL-C levels, and in Hispanic groups leg/whole ratio was non-significantly correlated with LDL-C levels.

Leg fat and metabolic syndrome

Similar to the pattern of association as observed in Supplementary Table 2, leg FM and FM % were associated with increased odds of MetS when trunk fat indices were not controlled for (Supplementary Table 3). After further adjustment for trunk FM or trunk FM%, associations of the opposite direction were observed between leg fat indices and MetS risk (Table 3). Significant linear trends were observed between higher leg FM% and increased odds of MetS among all three ethnic groups, although leg FM was non-significantly associated lower odds of MetS in these groups. Moreover, in all multivariate-adjusted models, odds of MetS was consistently lower across higher quintiles of the leg/whole and leg/trunk ratios. Regardless of ethnicity, participants in the highest quintile of leg/whole and leg/trunk ratios had dramatically lower odds of MetS (all ORs < 0.1 with significant Bonferroni-corrected *P* values for trend).

DISCUSSION

In this large nation-representative U.S. population we found that, regardless of ethnicity, leg fat indices tended to correlate with favorable profiles of adiposity-related risk factors after controlling for trunk fat. In addition, leg/whole and leg/trunk ratios were strongly associated with favorable profiles of these factors and lower odds of metabolic syndrome. These results suggest that, for a given magnitude of central or whole body adiposity, a larger proportion of leg fat may have a protective effect on cardiometabolic health.

These results are consistent with the majority of previous studies using DXA or other imaging techniques to assess the contributions of leg fat on cardiometabolic risk factors and MetS. Williams et al. (5) firstly reported that the amount of leg fat was inversely correlated with blood pressure and serum lipid levels in 224 white women aged 17 to 77 years after adjusting for age, menopause status, and other fat-distribution variables. Subsequent studies conducted among white populations (8, 9, 11, 12, 14) or participants with unidentified ethnicity (6, 7, 10, 15-17) corroborated the favorable associations of leg fat or peripheral fat to central fat ratio with cardiometabolic risk factors, although most of these studies had small sample sizes that may explain null findings for some of the associations. Data for other ethnicities are rare. In two investigations conducted among Asian populations, a similar favorable association was observed between leg fat mass and a wide array of cardiometabolic risk factors (13, 18). Consistently, in a small sample of Japanese women Okura et al found that loss of leg fat was associated with adverse change of cardiometabolic risk factors (24). To our knowledge, the current study provided the first evidence in this regard for non-Hispanic blacks and Hispanics. These ethnic groups have different body fat distribution(19) and metabolic risk profiles(1) from non-Hispanic whites. For example, non-Hispanic blacks tend to have lower body fatness that non-Hispanic whites (25), and Hispanic males and females generally have higher body fatness than non-Hispanic whites and blacks (26, 27). With respect to metabolic risk, non-Hispanic blacks and Hispanics have higher prevalence of metabolic syndrome and its components than non-Hispanic whites (1). In the current investigation, although the strength and significance of associations may vary among non-Hispanic whites and blacks and Hispanics probably because of various sample sizes, we found consistent patterns of favorable associations between leg fat accumulation and cardiometabolic risk factors or metabolic syndrome in all three ethnic groups. In addition, the current study supports the notion that fat distribution as measured by leg to trunk fat and leg to whole-body fat ratios may provide substantially additional information in reflecting the severity of obesity beyond that of absolute amount of fat accumulation

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within specific regions of the body. Overall, all existing evidence consistently suggests that, in various ethnicities, increased peripheral fat mass accumulation, as well as peripheral to central fat mass ratio, may add to the prediction of insulin sensitivity over visceral adipose tissue and central fat mass alone.

The biological mechanisms for the potentially beneficial effects of leg fat accumulation on adiposity-related risk factors and risk of MetS are not entirely clear. Goodpaster et al (28) found that the vast majority of leg fat is located in subcutaneous adipose tissues, which may serve as a metabolic sink where free fatty acid (FFA) and glycerol are stored as triglycerides to buffer an energy surplus (29, 30). For given levels of trunk or whole body fat, a relatively larger amount of leg fat would lead to decreased accumulation of ectopic fat at undesirable sites (31). In addition, evidence shows that adipocytes in the gluteal or femoral region are less sensitive to factors stimulating lipolysis and have lower rate of lipolysis than in abdominal regions (32, 33). Moreover, basal FFA turnover rate is lower in peripheral-obese women than in central-obese women (34), and a greater uptake of circulating FFA was observed in femoral fat than in abdominal fat (35). As a result, compared to abdominal fat, high leg fat accumulation may lead to lower FFA concentrations in the portal vein, decreased triglyceride synthesis, and increased hepatic insulin clearance. Besides FFA, in comparison to visceral adipose tissue, peripheral adipose tissue also secrets lower levels of other detrimental adipokines, including tumor necrosis factor alpha (TNF-α) and plasminogen activator inhibitor-1(PAI-1), but higher levels of adiponectin (36-39). Gene expression of metabolic enzymes and related signaling proteins were also documented to be regionally different (40). These mechanisms collectively may underlie the protective effects of leg fat.

The primary limitation of our study is the use of cross-sectional study design, which prohibits us from inferring causality in the associations between leg fat and the cardiometabolic risk factors or MetS. Also, DXA is unable to distinguish between subcutaneous and intramuscular fat in the legs or between visceral and subcutaneous fat in the trunk. Therefore, we were unable to ascertain whether the favorable effects of leg fat on cardiometabolic risk factors and MetS were due to subcutaneous or intramuscular fat, and we could not additionally adjust for abdominal visceral or subcutaneous fat. It is possible that the effects of leg fat on risk factors or MetS vary by anatomic site. These results warrant further confirmation using more sophisticated imaging methods in large prospective studies. Lastly, we did not examine the associations of interest among other ethnic groups, such as Native Americans and Asian Americans because of small sample size for these ethnic minorities. Nevertheless, the strengths of our study include the use of data from NHANES 1999-2004 surveys, which were based on very large nationally representative samples with standardized data collection methods. Therefore, our results are more generalizable than those from previous studies. In addition, we carefully adjusted for potential confounders and excluded participants who took medications that lower the levels of cardiometabolic risk factors to minimize the strong confounding by existing chronic diseases.

In conclusion, in this large, nationally representative population, we demonstrate favorable associations of leg fat with a number of adiposity-related risk factors and risk of MetS after controlling for trunk fat in non-Hispanic blacks and Hispanics, as well as in non-Hispanic whites. Moreover, regardless of ethnicity, fat distribution as reflected by leg/whole and leg/trunk fat ratios may be more biologically meaningful in evaluating the adverse effects of obesity than absolute fat depot in certain regions. Our findings may thus provide new insight into the role of adiposity in cardiometabolic risk.

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Supplementary Material

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Table 1

Characteristics of study participants by ethnicity[a], NHANES, 1999-2004

Characteristics[b]	Non-Hispanic white (n = 4472[c])	Non-Hispanic black (n = 1683[c])	Hispanic groups (n = 2647[c])
Weighted percentage (%)	74.3	10.7	15.0
Unweighted percentage (%)	50.8	19.1	30.1
Age (yr)	43.2 (0.3)	38.4 (0.2)	37.4 (0.6)
Male (%)	2267 (49.3)	878 (48.7)	1378 (52.0)
BMI (kg/m^2)	27.0 (0.1)	28.7 (0.2)	27.8 (0.2)
Waist circumference (cm)	94.0 (0.3)	94.1 (0.5)	93.4 (0.5)
Whole body FM (kg)	26.8 (0.2)	28.0 (0.3)	25.8 (0.3)
Whole body FM%	33.1 (0.2)	32.2 (0.2)	33.5 (0.2)
Trunk FM (kg)	13.0 (0.1)	12.8 (0.2)	12.9 (0.2)
Trunk FM%	32.3 (0.2)	31.4 (0.2)	33.7 (0.3)
Leg FM (kg)	9.5 (0.1)	10.7 (0.1)	8.7 (0.1)
Leg FM%	35.3 (0.2)	34.5 (0.3)	34.6 (0.2)
Education (%)			
High school and below	1885 (39.2)	960 (55.5)	1981 (66.2)
College	1339 (31.3)	491 (30.4)	477 (23.3)
College graduate and above	1248 (29.5)	232 (14.1)	189 (10.5)
Smoking status (%)			
Never smoked	2249 (51.8)	1036 (63.7)	1687 (65.1)
Past smoker	1180 (23.8)	219 (11.1)	579 (18.7)
Current smoker	1043 (24.4)	428 (25.2)	381 (16.2)
Alcohol use (%)			
Non-drinkers	1361 (27.8)	685 (40.2)	956 (32.6)
1-3 drinks/day	2427 (55.3)	773 (46.5)	1026 (39.8)
4+ drinks/day	684 (16.9)	225 (13.3)	665 (27.6)
Moderate to vigorous physical activity (%)[d]	2989 (70.5)	889 (54.6)	1238 (53.6)
Cardiometabolic risk factors[e]			
SBP (mmHg)	120.0 (0.4)	122.6 (0.5)	118.1 (0.7)
DBP (mmHg)	72.3 (0.3)	73.6 (0.4)	70.6 (0.4)
TC (mg/dL)	203.3 (0.9)	191.2 (1.2)	197.6 (1.4)
LDL-C (mg/dL)	123.6 (0.9)	115.0 (1.4)	118.9 (1.5)
HDL-C (mg/dL)	52.7 (0.5)	54.7 (0.6)	48.9 (0.5)
TG (mg/dL)	142.5 (4.3)	101.5 (2.4)	148.3 (6.1)
CRP (mg/dL)	0.34 (0.01)	0.48 (0.03)	0.41 (0.03)
FBG (mg/dL)	96.4 (0.6)	94.7 (0.9)	98.1 (0.9)
FSI (μU/mL)	10.2 (0.3)	12.4 (0.4)	13.0 (0.5)

Abbreviations: BMI, body mass index; FM, fat mass; FM%, fat mass percent; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triacylglycerol; CRP, C-reactive protein; FBG, fasting blood glucose; FSI, fasting serum insulin.

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[a] Hispanic groups include American Mexican and other Hispanic groups in the NHANES surveys.

[b] Values are mean (SE) for continuous variables and numbers (weighted percentage) for categorical variables.

[c] Unweighted number of participants.

[d] Based on non-missing data only.

[e] n = 8420 for SBP; 8383 for DBP; 8297 for TC and HDL-C; 3782 for LDL-C; 4056 for TG; 4104 for FBG; 4046 for FSI; and 8340 for CRP.

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Table 2

Trunk fat-adjusted Pearson correlation coefficients[a] between leg fat indices and adiposity-related risk factors, by ethnicity.

	SBP (mmHg)	DBP (mmHg)	TC (mg/dL)	LDL-C (mg/dL)	HDL-C (mg/dL)	TG (mg/dL)	FBG (mg/dL)	FSI (uU/mL)	CRP (mg/dL)
Non-Hispanic white[b]									
Leg FM, kg	-0.05	-0.05	-0.03	-0.05	0.13[f]	-0.15[f]	-0.08	-0.04	0.002
Leg FM%	-0.06	-0.06	-0.05	-0.08	0.17[f]	-0.17[f]	-0.05	-0.05	-0.02
Leg/Whole	-0.13[f]	-0.14[f]	-0.19[f]	-0.21[f]	0.34[f]	-0.36[f]	-0.19[f]	-0.35[f]	-0.26[f]
Leg/Trunk	-0.15[f]	-0.16[f]	-0.21[f]	-0.23[f]	0.36[f]	-0.38[f]	-0.20[f]	-0.40[f]	-0.30[f]
Non-Hispanic black[c]									
Leg FM, kg	-0.05	-0.07	0.05	0.12	0.04	-0.06	-0.07	0.02	0.09
Leg FM%	-0.05	-0.08	0.01	0.06	0.07	-0.10	-0.08	-0.05	-0.002
Leg/Whole	-0.12[f]	-0.12[f]	-0.11[f]	-0.06	0.25[f]	-0.29[f]	-0.20[f]	-0.33[f]	-0.21[f]
Leg/Trunk	-0.14[f]	-0.15[f]	-0.14[f]	-0.11	0.29[f]	-0.33[f]	-0.23[f]	-0.41[f]	-0.29[f]
Hispanic groups[d]									
Leg FM, kg	-0.08	-0.06	-0.03	-0.02	0.07	-0.13[f]	-0.12	-0.06	0.04
Leg FM%	-0.07	-0.07	-0.04	-0.04	0.14[f]	-0.18[f]	-0.11	-0.10	0.02
Leg/Whole	-0.14[f]	-0.16[f]	-0.12[f]	-0.12	0.25[f]	-0.29[f]	-0.19[f]	-0.29[f]	-0.18[f]
Leg/Trunk	-0.15[f]	-0.19[f]	-0.14[f]	-0.15[f]	0.29[f]	-0.33[f]	-0.20[f]	-0.34[f]	-0.23[f]
Total[e]									
Leg FM, kg	-0.03	-0.05	-0.03	-0.02	0.13[f]	-0.15[f]	-0.09[f]	-0.04	0.02
Leg FM%	-0.03	-0.06[f]	-0.05	-0.06	0.16[f]	-0.19[f]	-0.06	-0.07	-0.01
Leg/Whole	-0.13[f]	-0.14[f]	-0.17[f]	-0.18[f]	0.32[f]	-0.34[f]	-0.19[f]	-0.34[f]	-0.24[f]
Leg/Trunk	-0.15[f]	-0.16[f]	-0.19[f]	-0.21[f]	0.35[f]	-0.37[f]	-0.20[f]	-0.40[f]	-0.29[f]

Abbreviations: FM, fat mass; FM%, fat mass percent; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triacylglycerol; FBG, fasting blood glucose; FSI, fasting serum insulin; CRP, C-reactive protein.

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[a] Pearson correlation coefficients were adjusted for age (yrs), gender (men, women), education (high school or below, any college, and college graduate or above), regular moderate-to-vigorous physical activity (yes, no), smoking status (nonsmoker, past smoker, or current smoker), and alcohol consumption (nondrinker, 1-3 drinks/day, or ≥4 drinks/day), as well as trunk FM when modeling association for leg FM or trunk FM% when modeling association for leg FM%. Ethnicity was further adjusted for when examining these correlations in total population.

[b] For non-Hispanic white, n = 4316 for SBP, 4293 for DBP, 4270 for TC and HDL, 1958 for LDL, 2080 for TG, 2091 for FBG, 2075 for FSI, and 4285 for CRP.

[c] For non-Hispanic black, n = 1582 for SBP, 1577 for DBP, 1523 for TC and HDL, 700 for LDL, 762 for TG, 781 for FBG, 759 for FSI, and 1535 for CRP.

[d] Hispanic groups included Mexican Americans and other Hispanic groups. N = 2522 for SBP, 2513 for DBP, 2504 for TC, 1124 for LDL, 1214 for TG, 1232 for FBG, 1212 for FSI, and 2520 for CRP.

[e] Included non-Hispanic White, non-Hispanic Black, and Hispanic groups.

[f] Significant Bonferroni-corrected P value ($P < 0.00028$).

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Table 3

Multivariate-adjusted odds ratio (95% CI) for metabolic syndrome by leg fat indices, by ethnicity.

	Non-Hispanic White			Non-Hispanic Black			Hispanic groups			Total[f]			
	Q1	**Q3**	**Q5**	**Q1**	**Q3**	**Q5**	**Q1**	**Q3**	**Q5**		**Q1**	**Q3**	**Q5**
Leg FM, kg										Leg FM, kg			
MetS/Control[a]	59/343	107/296	166/237	7/138	26/119	46/99	47/187	78/156	101/133	MetS/Control[a]	113/668	211/571	313/469
Multivariate-adjusted[b]	1.0	0.64 (0.50, 0.81)	0.41 (0.24, 0.71)	1.0	1.91 (0.65, 5.63)	0.70 (0.20, 2.44)	1.0	0.53 (0.32, 0.89)	0.32 (0.19, 0.53)	Model 1[d]	1.0	0.62 (0.40, 0.96)	0.38 (0.22, 0.68)
Leg FM%										Leg FM%			
MetS/Control[a]	67/335	131/272	134/269	7/138	40/105	41/104	50/184	99/135	96/138	MetS/Control[a]	124/657	270/512	271/511
Multivariate-adjusted[b]	1.0	0.40 (0.27, 0.62)	0.27[c] (0.18, 0.41)[d]	1.0	0.53 (0.10, 2.81)	0.06 (0.01, 0.42)[d]	1.0	0.50 (0.27, 0.90)	0.18[c] (0.08, 0.38)[d]	Model 1[b]	1.0	0.42 (0.26, 0.67)	0.22[c] (0.11, 0.44)[d]
Leg/Whole										Leg/Whole			
MetS/Control[a]	212/190	104/299	27/376	57/88	29/116	11/134	132/102	78/156	28/206	MetS/Control[a]	401/380	211/571	66/716
Multivariate-adjusted[b]	1.0	0.28 (0.22, 0.36)	0.04[c] (0.02, 0.06)[d]	1.0	0.33 (0.21, 0.51)	0.06[c] (0.03, 0.11)[d]	1.0	0.30 (0.22, 0.42)	0.08[c] (0.04, 0.17)[d]	Model 1[b]	1.0	0.29 (0.20, 0.41)	0.05[c] (0.03, 0.08)[d]
Leg/Trunk										Leg/Trunk			
MetS/Control[a]	215/187	103/300	24/379	62/83	23/122	7/138	138/96	79/155	25/209	MetS/Control[a]	415/366	205/577	56/726
Multivariate-adjusted[b]	1.0	0.25 (0.22, 0.28)	0.03[c] (0.02, 0.04)[d]	1.0	0.19 (0.12, 0.33)	0.04[c] (0.01, 0.10)[d]	1.0	0.26 (0.18, 0.39)	0.07[c] (0.02, 0.24)[d]	Model 1[b]	1.0	0.24 (0.17, 0.35)	0.04[c] (0.02, 0.06)[d]

Abbreviations: FM, fat mass; FM%, fat mass percent; MetS, metabolic syndrome.

[a] Number of metabolic syndrome cases and controls were calculated based on the first imputation dataset. We only included subjects who had non-missing MetS components in this analysis.

[b] Adjusted for age (yrs), gender (men, women), education (high school or below, any college, and college graduate or above), regular moderate-to-vigorous physical activity (yes, no), smoking status (nonsmoker, past smoker, or current smoker), alcohol consumption (nondrinker, 1-3 drinks/day, or ≥4 drinks/day), self-reported cardiovascular disease (yes, no), and family history of diabetes or cardiovascular disease (yes, no), as well as trunk FM when modeling association for leg FM or trunk FM% when modeling association for leg FM%. Ethnicity was further adjusted for when examining these correlations in total population.

[c] Significant Bonferroni-corrected P value for odds ratios comparing extreme quintiles ($P < 0.00028$).

[d] Significant Bonferroni-corrected P value for linear trend ($P < 0.00028$).

[f] Included non-Hispanic white, non-Hispanic black, and Hispanic groups.